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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/695,437	10/24/2000	Carl W Anderson	BSA 01-02	2813

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EXAMINER	
PROUTY, REBECCA E	
ART UNIT	**PAPER NUMBER**
1652	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/695,437	Anderson et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication app ars on the cover she t with th correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Apr 28, 2003

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-111 is/are pending in the applica

4a) Of the above, claim(s) 1-22, 25-28, 53-98, and 106-111 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 23, 24, 29-52, and 99-105 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, Claims 23-52 and 99-105 and the peptide substrate species of SEQ ID NO:11 in Paper No. 12 is acknowledged.

Claims 1-22, 25-28, 53-98, and 106-111 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 12. Note Claims 25-28 are withdrawn as reciting features not found in the elected species.

Claims 23, 24, 29-33, 36-52, and 99-105 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23, 36, and 99 (upon which Claims 24, 29-33, 37-52 and 100-105 depend) are confusing in the recitation of "phosphorylation site consensus sequence motif" as it fails to define for what kinase. There are many different kinases which have a wide variety of different phosphorylation site consensus sequence motifs. For purposes of examination it is assumed that this refers to a DNA-PK phosphorylation site consensus sequence motif i.e., E/QS/TQ, S/TQE/Q, E/QQS/T, or QS/TE/Q.

Claim 24 is confusing in the recitation of "comprises 1 to 4 amino acids" as the use of the term comprises with a specific

length limitation is confusing. The term comprises suggests that the spacer could be any length of amino acids yet if this is true, the claims is not further limiting of Claim 23. If the claim is limited to first spacers of 1-4 amino acids in length, it is suggested that "comprises" be replaced with "consists of". For examination the suggested language is assumed to be intended.

Claims 30, 32, 41, and 43 (upon which Claims 33 and 44 depend) are confusing in the recitation of several peptides with the recited Markush group which do not meet the limitations of the generic claim from which they depend (i.e., Claims 23 or 36). The Markush group of these claims includes SEQ ID NO:2 which includes two DNA-PK phosphorylation consensus sequences (i.e. ESQ at residues 3-5 and SQE at residues 15-17) and thus has a spacer sequence which does not meet the limitation of "any combination of amino acids which does not provide a phosphorylation site consensus sequence motif" and SEQ ID NOS:6 and 14 neither of which has an enhancer amino acid (E or Q) immediately adjacent to the phosphate accepting S/TQ or QS/T pair as required by Claims 23 and 36.

Claims 31 and 42 (upon which Claims 32-33 and 43-44 depend) are vague and indefinite in the recitation of "variant of the amino acid sequences found at the amino terminus of" as the meets and bounds of the term variant is unclear. How similar to the

amino-terminus of human or mouse p53 must a peptide be to within the scope of the term "variant".

Claims 45 and 102 (upon which Claims 46-47 depend) is indefinite in the recitation of "similar composition to the synthetic peptide" as the meets and bounds of the term "similar" are unclear. How many and what types of differences are within the scope of the term similar and which are excluded?

Claim 48 (upon which Claim 49 depends) lacks antecedent basis for "said negative control peptide". Did applicants intend this claim to depend from Claim 45?

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23, 24, and 29-35 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Lees-Miller et al. (1992). Note this rejection is made under 102(b) for Claims 24 and 29 as these claims recite limitations which are not supported by grandparent application 08/132,284. The grandparent application fails to support the specific limitations of the first spacer being from

1-4 amino acids in length (Claim 24) and the first and second spacer sequences excluding serine, threonine and tyrosine (Claim 29).

Lees-Miller teach a large number of synthetic peptide substrates of DNA-PK (see table 1) including the peptide of SEQ ID NO:11 (peptide 15) and the use of these substrates for the assay of DNA-PK activity. SEQ ID NO:11 is a variant of amino acid residues 11-24 of human p53 including Ser15, has a 4 aa first spacer sequence and includes no Ser, Thr, or Tyr residues in either spacer sequence. Lees-Miller further teach the use of SEQ ID NO:20 (peptide 19) as a negative control peptide for DNA-PK assays (see pg 5046).

Claims 23 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Vojtesek et al.

Vojtesek et al. teach a composition comprising the human p53 peptide fragments of residues 1-37 and 1-53 (see page 241). As these fragments comprise all of SEQ ID NO:1 they have all the features recited in Claim 23 and anticipate the instant claims. It should be noted that the recitation of intended use of the composition i.e., "for detecting and quantitating DNA-PK activity in a biological sample" has no patentable weight as it does not provide any limitation on the claimed composition.

Claims 23, 24 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al.

Lam et al. teach a composition comprising a synthetic peptide variant of mouse p53 residues 16-34 linked to agarose (called Pro-17-Gly by Lam et al.). This peptide comprises a 2 amino acid first spacer sequence, the sequence SQE, a second spacer sequence of 14 amino acids and a tag (agarose beads) and thus anticipates the instant claims. t should be noted that the recitation of intended use of the composition i.e., "for detecting and quantitating DNA-PK activity in a biological sample" has no patentable weight as it does not provide any limitation on the claimed composition.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and

potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 24, 36-40, 45, 46, 48, 50-52, 99-100, and 102-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. in view of Glass et al.

Chen et al. teach that a synthetic peptide corresponding to SV40 T antigen residues 661-674 is phosphorylated well by DNA-PK as well as assays for DNA-PK phosphorylation which comprise a peptide substrate, the enzyme, ^{32}P-ATP, calf-thymus DNA and buffers. the 661-674 peptide has the sequence TGIDSQSQGSPQAP and thus comprises a first amino acid spacer, a QSQ sequence, and a second amino acid spacer. Thus this peptide meets all limitations of the synthetic peptide recited in Claims 23, 36 and 99 except for the presence of a tag moiety which can be used to separate the labeled peptide from the ^{32}P-ATP following phosphorylation by DNA-PK.

Glass et al. teach the use of *in vitro* synthetic peptide substrates for the specific assay of protein kinases and teach that one means of separating labeled peptides form the unused labeled phosphate donor is the use of phosphocellulose paper to bind a the labeled peptide. Glass et al. teach that use of this method requires that the peptide substrate contain at least two basic residues (i.e., Lys or Arg) for the peptide to be retained

on the phosphocellulose paper. Glass et al. teach that this method of protein kinase assay is simple and accurate and should be useful for the assay of a variety of protein kinases.

Chen et al. teach that DNA-PK is an enzyme which likely regulates nuclear functions and thus the skilled artisan would clearly desire a simple and accurate *in vitro* assay for its activity. Therefore, it would have been obvious to use the 661-674 TAg peptide of Chen et al. as a peptide substrate in an assay format as disclosed by Glass et al. As the sequence of this peptide does not include the two necessary basic residues, it would have been obvious to one of skill in the art to add two basic lysine or arginine residues to this peptide and to use this peptide in a assay format as taught by Glass et al. Furthermore, it would have been obvious to one of ordinary skill in the art to include all components (peptide substrate, phosphate donor, enzyme, etc.) necessary for such an assay as taught by Chen et al. together in a kit for the added convenience of the user. The inclusion of a negative control peptide substrate within such a kit would have been further obvious to one of skill in the art. The skilled artisan would have used a peptide highly similar to that of the 661-674 peptide but lacking an essential feature necessary for phosphorylation by DNA-PK. As Chen et al. teach

the importance of the SQ sequence for phosphorylation, it would have been obvious to one of ordinary skill to replace one or both of these residues with a similar amino acid (for example alanine for serine or glutamate for glutamine) which would eliminate the SQ phosphorylation site. Therefore, all of Claims 23, 24, 36-40, 45, 46, 48, 50-52, 99-100, and 102-105 would have been obvious to one of skill in the art at the time of the invention.

Claims 36-52 and 99-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lees-Miller et al. (1992).

Lees-Miller et al. is discussed above.

It would have been obvious to one of ordinary skill in the art to include all components (peptide substrate, phosphate donor, enzyme, etc.) necessary for the DNA-PK assays of Lees-Miller et al. together in a kit for the added convenience of the user. The inclusion of a negative control peptide substrate such as peptide 19 (SEQ ID NO:20) or other peptides of Lees-Miller et al. similar to peptide 15 which are incapable of being phosphorylated by DNA-PK such as peptide 5 amino acids 11-24 within such a kit would have been further obvious to one of skill in the art. Therefore, all of Claims 36-52 and 99-105 would have been obvious to one of skill in the art at the time of the invention.

The references lined thru on Applicants information disclosure statement were not considered as copies of these references are not found in that parent applications. Applicant is requested to provide copies of these references if they wish to have them considered in the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652